CORRESPONDENCE

Eradication of multiresistant *Salmonella* Hadar convalescent-phase carriage with azithromycin

For over a decade, fluoroquinolones have been the standard treatment of non-typhoid salmonella infections. They have also been reported to reduce the occurrence or duration of convalescent carriage [1,2], and consequently to reduce the risk of relapse or dissemination [3]. However, given the extensive use of these drugs in both veterinary and human practice, both in vitro resistance and clinical failures occur, especially with some serotypes (*Salmonella* Hadar, *S.* Typhimurium, *S.* Choleraesuis) [4,5]. Hitherto, no alternative antibiotics have been available to clear salmonella carriage in cases of fluoroquinolone resistance.

Azithromycin is highly effective against intracellular salmonellae [6] and has been used successfully in the acute phase of typhoid fever [7,8], even in cases of multiresistance [7,8]. It has also cleared *S.* Typhi from stools [8]. However, the clinical efficacy of azithromycin in non-typhoid infections is not as well documented. We report a case of multiresistant *S.* Hadar convalescent carriage following an invasive infection in an immunocompetent woman that was cured with a single course of azithromycin.

A 31-year-old woman with no significant past medical history presented with three days of diarrhea, fever and abdominal pain. Her admission temperature was 40 °C, her pulse was 110/min, and her blood pressure was 120/60 mmHg. Clinical examination revealed a poor general condition, dehydration, and abdominal tenderness without rebound. The white blood cell count was 12×10^9/L (9800 neutrophils), and the C-reactive protein level was 175 mg/L. Blood and stool cultures grew *S.* Hadar resistant to amoxicillin, nalidixic acid and pefloxacin, and with low susceptibility to ciprofloxacin (minimal inhibitory concentration (MIC) of 0.5 mg/L). The patient was HIV negative, and other immunodeficiency diseases were ruled out. Abdominal ultrasonography was normal. The presumed source of contamination was chicken eaten at an Asian restaurant the day before the onset of illness. Ciprofloxacin (200 mg twice daily) was given intravenously for 3 days, without clinical effect. Intravenous ceftriaxone was substituted (2 g daily for 8 days), and the patient improved within 24 h. Upon complete clinical recovery, she was discharged, but *S.* Hadar persisted in semimonthly stool cultures 2 months after discharge. Given the risk of a relapse or exposure of either family or colleagues, azithromycin (500 mg daily for 5 days) was proposed, in spite of the high MICs (2 and 4 mg/L, respectively) of two *S.* Hadar strains tested by the agar dilution method. However, stool cultures became negative on day 12 and remained free of *S.* Hadar during a follow-up period of 6 months. Tolerance of azithromycin was excellent.

S. Hadar is commonly resistant in vitro to β-lactams, nalidixic acid and fluoroquinolones [4]. Non-Typhi salmonella resistance to fluoroquinolones mainly derives from mass use, in both animals and humans [4,5]. As a result, treatment of invasive diseases in humans has become more difficult, as shown in our case.

Convalescent carriage is well documented in salmonella infections and reaches rates of 20% in non-Typhi strains [10]. Usually no treatment is required, except in rare epidemiologic or clinical situations, e.g. the institutionalized elderly [3], infants or patients with sickle cell disease or HIV infection. We believe, however, that persistence in stools of multiresistant *Salmonella* after a severe invasive infection is also an indication for treatment, even in immunocompetent patients. Nevertheless, attempts at eradication are difficult with multiresistant strains.

Azithromycin, a drug effective in vitro in eradicating intracellular *Salmonella* [6], produced bacterial cure (negative stool cultures) in 100% of cases of enteric fever [8]. However, in another clinical trial, it was no better than placebo in clearing non-Typhi salmonellae from stools [9], but most of those patients were lost to follow-up [9].

Although cut-offs for the MIC of azithromycin were not determined, its clinical efficacy could be explained by very high intracellular concentrations, regardless of the high serum MIC levels in the reported case. In our patient, carriage eradication was attributed to azithromycin, although spontaneous clearance cannot be ruled out [10].

We therefore suggest that this antibiotic warrants further investigation in the treatment of chronic *Salmonella* carriers.

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REFERENCES

1. Sammalkorpi K, Lähdevirpa J, Mäkelä T, Rostila T. Treatment of chronic Salmonella carriers with ciprofloxacin. *Lancet* 1987; 2: 164–5.
2. Raymond J, Moulin F, Badoual J, Gendrel D. Eradication of convalescent-phase Salmonella carriage in children with two oral doses of pefloxacin. *Eur J Clin Microbiol Infect Dis* 1994; 13: 307–10.
3. Ahmad F, Bray G, Prescott RW *et al.* Use of ciprofloxacin to control a Salmonella outbreak in a long-stay psychiatric hospital. *J Hosp Infect* 1991; 17: 171–8.
4. Threlfall EJ, Ward LR, Skinner JA *et al.* Increase in multiple antibiotic resistance in non typhoidal Salmonellas from humans in England and Wales. *Microb Drug Resist* 1997; 3: 263–6.
5. Chiu CH, Wu TL, Su LH *et al.* The emergence in Taiwan of fluoroquinolone resistance in *Salmonella enterica* serotype Choleraesuis. *N Engl J Med* 2002; 346: 413–19.
6. Chiu CH, Lin TY, Ou JT. In vitro evaluation of intracellular activity of antibiotics against non-typhoid Salmonella. *Int J Antimicrob Agents* 1999; 12: 47–52.
7. Butler T, Sridhar CB, Daga MK *et al.* Treatment of typhoid fever with azithromycin versus chloramphenicol in a randomized multicentre trial in India. *J Antimicrob Chemother* 1999; 44: 243–50.
8. Girgis NI, Butler T, Frenck RW *et al.* Azithromycin versus ciprofloxacin for treatment of uncomplicated typhoid fever in a randomized trial in Egypt that included patients with multidrug resistance. *Antimicrob Agents Chemother* 1999; 43: 1441–4.
9. Chinh NT, Parry CM, Ly NT *et al.* A randomized controlled comparison of azithromycin and ofloxacin for treatment of multidrug-resistant or nalidixic acid-resistant enteric fever. *Antimicrob Agents Chemother* 2000; 44: 1855–9.
10. Buchwald DS, Blaser MJ. A review of human salmonellosis. II. Duration of excretion following infection with nontyphi Salmonella. *Rev Infect Dis* 1984; 6: 345–56.